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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
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EXAMINER	
ZAGHMOUNT,O	
ART UNIT	**PAPER NUMBER**
1649	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary

Application No.	Applicant(s)
08/992,914	Watanabe et al.
Examiner	**Group Art Unit**
Ousama Zaghmout	1649

☒ Responsive to communication(s) filed on *Dec 18, 1997*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-39* is/are pending in the applicat

Of the above, claim(s) *19-28 and 37-39* is/are withdrawn from consideration

☒ Claim(s) *6, 9, 12, 13, 17, and 18* is/are allowed.

☒ Claim(s) *1-5, 7, 8, 10, 11, 14-16, and 29-36* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 9

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Detailed Action

Claims 1-39 are pending. Group I, claims 1-18, 29-36 were elected by the Applicants with traverse in the restriction requirements response which was filed 8/3/98. As such, claims 19-28, 37-39 were drawn from further consideration. The argument made by the Applicants regarding the rejoining of groups I, III, IV and V is acknowledged. As stated in the previous Office Action, in each one of these inventions, different sets of nucleotide sequence are produced. As such, each sequence gets isolated will require an independent search. Additionally, if the nucleotide sequence is different, the product will be different and the use may be different too. Therefore, these groups are drawn to a completely different inventions with completely different products, and searching for the claims of each invention will be completely different. Therefore, the groupings of these inventions into groups I, III, IV and V is maintained.

The CRF submitted by the applicants is technically bad. Please see attached forms for compliance with the sequence requirements.

Notice of draftsperson's patent drawing review (PTO 948) is enclosed.

The IDS is noted.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1st Paragraph

Claims 1-18, 29-36 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. In the instant disclosure, the applicants did disclose only the sequences cited in SEQ ID NO: 1-8 which encode for raffinose synthase. No other sequences which encode raffinose synthase from plants were disclosed. In light of the fact that these genes which encode raffinose synthase are recently being isolated from plant, there is not information about it in literature to predict if genes within this genus are very similar and can be isolated easily. Therefore, a written description of the other claimed sequences of raffinose synthase should be disclosed to overcome this rejection. See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA

from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. 35 USC 112 requires inter alia that a patent specification contain a written description of the invention and the manner and process of making and using it "in such full clear and concise terms as to enable one skilled in the art ... to make and use" the invention. Case law has made it clear that the requirements for a "written description" and an "enabling disclosure" are separate. For example, where a specification contains sufficient information to enable a skilled chemist to produce a particular compound because it gives detailed information on how to produce analogous compounds but it makes no reference to the compound in question, the "written description" requirement has not been met even though the description may be enabling.

The separateness of the two requirements has been emphasized in the biotechnology area by two cases. Both cases involved interferences in which the count in question related to a strand of DNA. In one case Fiers v. Sugamo[25 USPQ2d 1601 (Fed. Cir. 1993], :"An adequate description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it; what is required is a description of the DNA itself." In the Fiers case, convention priority was denied to a claim to a DNA sequence coding for a specified protein because of the absence of the actual sequence of the DNA in the priority documents. A similar situation occurred in Fiddes v.Baird [30 USPQ2d 1481 (Bd. of Appeals 1993).] where the Board of Appeals stated that "knowledge of amino

acid sequence of a protein coupled with the established relationship in the genetic code between a nucleic acid and a protein it encodes would not establish possession of a gene encoding that protein."

Claims 1-5, 7-8, 10-11, 14-16, 29-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabled for isolation of the sequences identified in SEQ ID Nos: 1-8 and the expression of SEQ ID NO: 8 in transgenic mustard and somatic embryos of soybean, does not reasonably provide enablement for the isolation of all nucleotide sequences, DNA fragments, any amino acid sequence derived by deletion, replacement, modification or addition of one or several amino acids in the amino acid sequence of SEQ ID Nos: 1 and 3 which encode raffinose synthase from all plant species and for the expression of sequences identified in SEQ ID Nos: 1-7 and all other claimed but not disclosed sequences which encode raffinose synthase in transgenic plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The breadth of the claims are not commensurate in scope with the enabling support provided. Applicants broadly claim all nucleotide sequences which encode raffinose synthase from all plant species and the expression of sequences identified in SEQ ID Nos: 1-7. Furthermore, Applicants claim all DNA fragments and any amino acid sequence derived by deletion, replacement, modification or addition of one or several amino acids in the amino acid sequence of SEQ ID Nos: 1 and 2 which encode raffinose synthase, and all other claimed but

not disclosed sequences which enocde raffinose synthase in transgenic plants. However, in the instant disclosure, applicants provide and explicitly demonstrate only the isolation of the nucleotide sequence identified in SEQ ID No: 1-8 and the expression of SEQ ID NO: 8 in transgenic mustard and transgenic soybean somatic embryo. The expression of the claimed DNA molecules in transgenic cells and plants by the applicants is very critical for the enablement of the claimed invention in the light of the fact that the process of transforming plants with individual genes to obtain desired phenotypes is unpredictable. Napoli et al. observed a reversible inhibition of expression of the desired gene, when introduced in sense orientation into a plant, so that the desired phenotype was not observed (The Plant Cell. 1989. Vol. 2: 278-289. see page 279, Abstract).

Furthermore, it is important to show traits encoded by the transgenes will be maintained in these transgenic cells and plants when they are used in breeding programs. This is important in the light of the fact that traits encoded by some transgenes have been shown to decline/or disappear stage thereafter. Carvalho et al. teach that expression of a transgenic glucanase was silenced in a homozygous transgenic tobacco line (T17). Carvalho et al. further teach that transgenic glucanase mRNA was detected at high level in the homozygous plant during the first 4 weeks of development. Carvalho et al. further teach that after 4 weeks, the mRNA level decreased gradually. In some Nicotiana sylvestris plants transformed with a p35S-chitinase gene the lower leaves showed a high chitinase content, whereas the upper leaves, formed later in development, showed low chitinase content and co-suppression of both the

transgenic and the endogenous chitinase gene (Carvalho et al. The EMBO Journal. 1992. Vol. 11: 2995-2602. The 4th paragraph under the Discussion section).

Furthermore, Applicant's disclosure does not provide a reliable procedure for producing protein from the claimed nucleotide sequence in E-coli. This is a very common problem in the expression of heterologous proteins in E. coli as taught by Ejdeback et al. (Protein Expression and Purification. 1997. Vol. 11: 17-25). Ejdeback et al. teach the effects of codon usage and vector-host combinations on the expression of spinach plastocyanin in E.coli. Ejdeback et al. teach that expression of heterologous proteins in E. coli can be difficult because of the differences in codon usage between E. coli and the organism from which the gene was obtained, as common codons in the latter might be rare codons in the former. Ejdeback et al. teach that rare codons are translated more slowly and stretches of rare codons are believed to cause ribosomes to stall, causing premature termination and/or less frequent initiation of translation (page 17, last paragraph on the right). Ejdeback et al. teach that since the ribosome covers a region of at least nine codons, numerous rare codons within this distance are proposed to be effective in slowing down the ribosome movement and the following ribosomes on the same mRNA. Ejdeback et al. teach that slower translation may also permit formation of secondary structures acting as termination signals or nuclease-sensitive sites on the mRNA. Altogether, this might result in a lower mRNA level and therefore a lower yield of the recombinant protein (page 18, first paragraph on the left) . Ejdeback et al. teach the usage of site-directed mutagenesis to introduce changes that affect

both mRNA and protein stability in order increase the level of expression (page 18, lines 15-16).

Applicants failed to address many of these important issues which are essential for the enablement of the claimed invention. Taken together, the instant disclosure lacks the proper and sufficient guidance to enable the claims as set forth. Thus it is not readily predictable that the genetic modification specifically disclosed will work with other claimed genes and in any plant species. Thus it is not readily predictable that the genetic modification specifically disclosed will work with other genes or other plants. Applicant has provided no specific guidance as to how to select genes which will give the desired effect or provided guidance with regard to selection of other plants and/or the technique to be used in the modification of these genetic modification of these plants. One wishing to practice the invention is left to proceed through trial-and-error to see what will work and what will not.

In view of the breadth of the claims, unpredictability, lack of guidance in the specification of the results as stated above, it is the examiner's position that one skilled in the art to which it pertains, or with which it is most nearly connected, could not practice the invention commensurate in scope with these claims without undue experimentations.

2nd Paragraph

Claims 5, 8, 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 8 are rejected as being vague and indefinite in failing to clearly define the metes and bounds of the claims. See *In re Hammack*, 427 F.2d 1378, 1382, 166 USPQ 204, 208 (CCPA 1970). The sequence of the claimed protein encompassed by subparagraph (b) is not adequately defined. These designated alterations to SEQ ID Nos: 1 and 3 are not defined by the specification. The specification does not provide a standard for ascertaining the requisite degree of modification, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 29 is rejected as being confusing as it is not clear which sequence is claimed in that "fragment". The length or sequence of the fragment is not specified .

Conclusion

Claims 1-18, 29-36 are deemed free of the prior art given the failure of the prior art to teach or suggest the particularly claimed DNA sequence identified in SEQ ID NOs: 1-8 and their usage in transformation experiments.

Claims 6, 9, 12, 13 17-18 are allowed.

Claim 29 is objected for depending on non-elected claim.

Future Correspondence

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Ousama M-Faiz Zaghmout whose telephone number is (703) 308-9438. The Examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Douglas Robinson, can be reached on (703) 308-2897. The fax phone number for the group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to THE MATRIX CUSTOMER SERVICE CENTER whose telephone number is (703) 308-0196.

Ousama M-Faiz Zaghmout Ph.D.

September 8, 1998

Douglas W. Robinson
Supervisory Patent Examiner
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